Effusion and Edema

Incidence and Management

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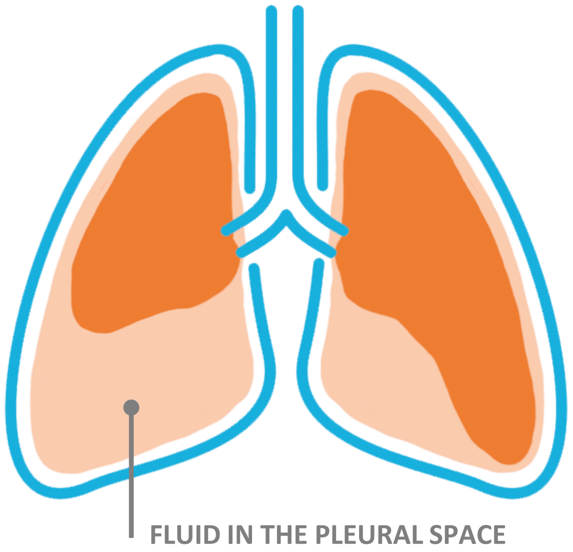
Objectives

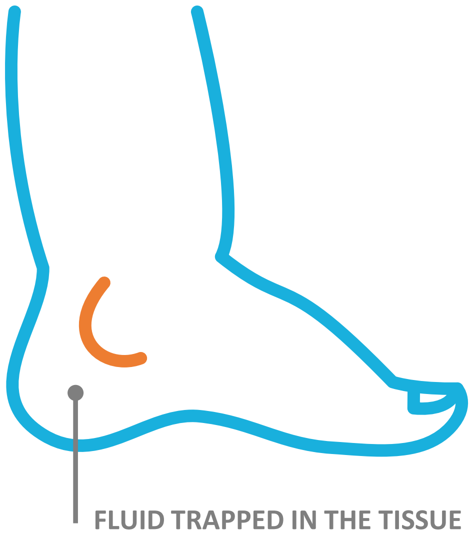
Effusion and Edema

- Review updated post-hoc analysis data on the incidence, onset, and duration of effusion and edema in the LOTIS-2 study
- Review the prescribing information and LOTIS-2 dose management of loncastuximab tesirine (Lonca) and discuss the adverse events management of effusion and edema

Effusion



Edema



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Indication and Usage

Indication for Loncastuximab Tesirine-lpyl

Loncastuximab tesirine is indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including DLBCL not otherwise specified, DLBCL arising from low-grade lymphoma, and high-grade B-cell lymphoma.

This indication is approved under accelerated approval based on overall response. Continued approval for this indication may be contingent upon verification and description of the clinical benefit in a confirmatory trial(s).

Warnings and Precautions

Effusion and Edema Warning from the Lonca Prescribing Information

Serious effusion and edema occurred in patients treated with loncastuximab tesirine. Grade 3 edema occurred in 3% (primarily peripheral edema or ascites) and Grade 3 pleural effusion occurred in 3% and Grade 3 or 4 pericardial effusion occurred in 1%.

Monitor patients for new or worsening edema or effusions. Withhold loncastuximab tesirine for Grade 2 or greater edema or effusion until the toxicity resolves. Consider diagnostic imaging in patients who develop symptoms of pleural effusion or pericardial effusion, such as new or worsened dyspnea, chest pain, and/or ascites such as swelling in the abdomen and bloating. Institute appropriate medical management for edema or effusions.

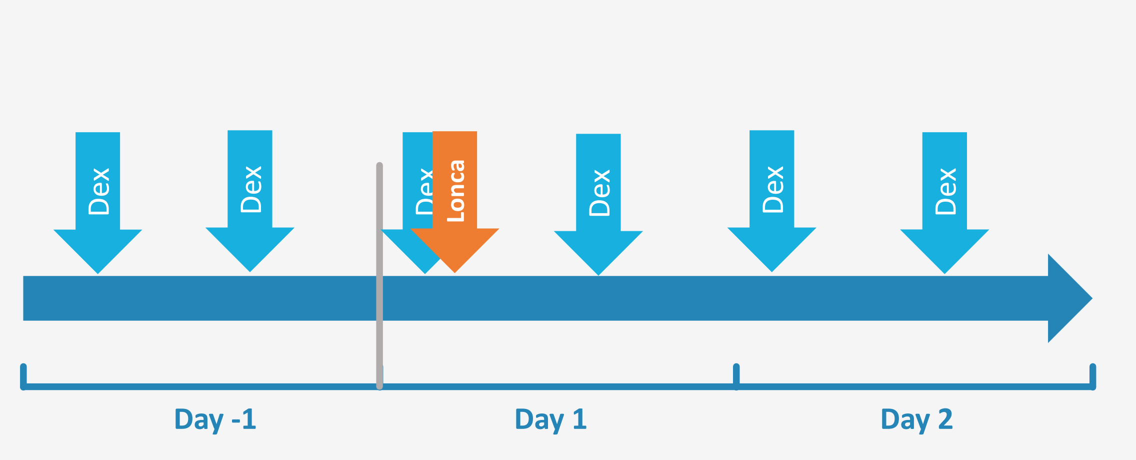
Premedication Recommendation

The loncastuximab tesirine prescribing information recommends dexamethasone premedication[1]

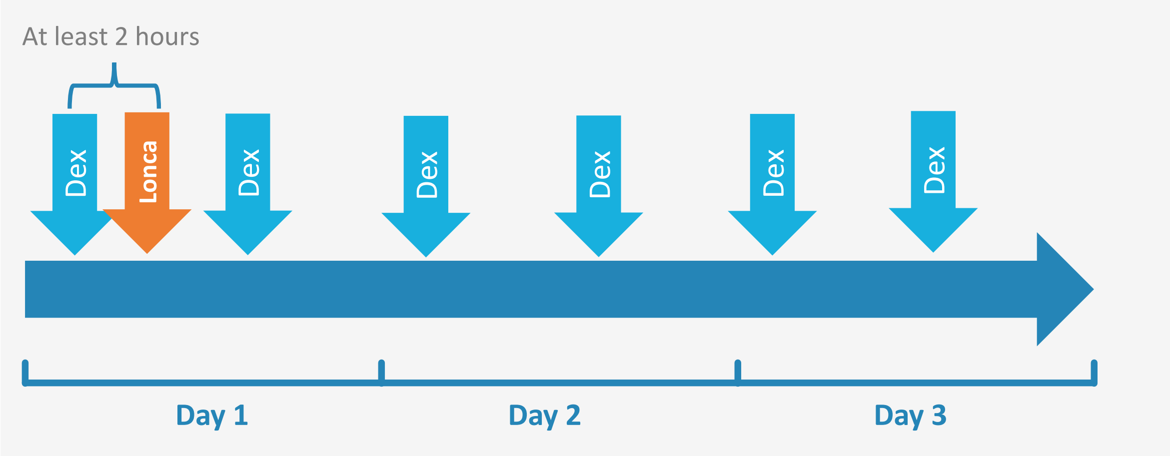
- Dexamethasone premedication is recommended to reduce the incidence and severity of pyrrolobenzodiazepine (PBD)-related adverse reactions, such as effusion and edema[2,3]

Dexamethasone Premedication Administration

If dexamethasone administration begins the day before Lonca:



If dexamethasone administration does not begin the day before Lonca:



Incidence, Onset, Duration, and Dose Modification for Effusion (LOTIS-2)

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All-Treated Population (N=145)[1,a]

Effusion

	Incidence	Onset (median)	Duration[b] (median)
Any grade	**11.7%** (n=17)	**52 Days** Range: 3-234	**20 Days** Range: 4-581
Grade ≥3	**2.8%** (n=4)	**118 Days** Range: 17-277	**20.5 Days** Range: 6-411

Onset: Any grade effusion typically developed within the first 3 cycles. Grade ≥3 effusion typically developed within the first 6 cycles[1]

Presentation: Presenting symptoms of pleural effusion included dyspnea (31.3%), cough (31.3%), and musculoskeletal chest pain (18.8%)[2,c]

Predisposing factors: No predisposing factors (including medical history, concomitant medications, or reported incidence of hypoalbuminemia) were identified between patients with or without reported effusion events[2,c]

Dose Modification Due to Effusion,

Subset of Patients with Effusion (n=17)[1,a]

Delayed	Reduced	Discontinued
11.8% (n=2)	**0%** (n=0)	**23.5%** (n=4)

1 of **2** patients (**50%**) who had a dose delay due to effusion were rechallenged with Lonca[2,c]

[a]Data cut-off: March 1, 2021. Post-hoc analysis.
[b]Missing end dates were imputed using the date of new anticancer therapy (NAT) for patients who received NAT or the end of study (EOS)/data cutoff date for patients who did not receive NAT for the calculation of the duration of adverse events. Partial end dates were imputed using the last month or day of a month bounded by EOS. Grade ≥3 duration calculated at the time of first occurrence to the adverse event resolved to grade ≤2. [c]Data cutoff: April 6, 2020. Post-hoc analysis.

Incidence, Onset, Duration, and Dose Modification for Edema (LOTIS-2)

All-Treated Population (N=145)[1,a]

Edema[b]

	Incidence	Onset (median)	Duration[c] (median)
Any grade	27.6% (n=40)	40 Days Range: 1-277	50.5 Days Range: 2-676
Grade ≥3	3.4% (n=5)	106 Days Range: 9-183	5 Days Range: 3-112

Onset: Any grade edema typically developed within the first 3 cycles. Grade ≥3 edema typically developed within the first 6 cycles[1]

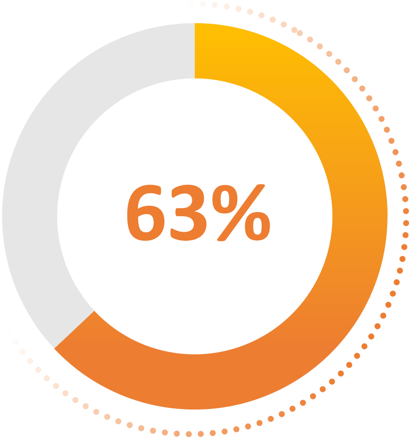
Presentation: Most patients with edema presented with peripheral edema (72.5%) and facial edema (17.5%)[2,d]

Predisposing factors: No predisposing factors (including medical history, concomitant medications, or reported incidence of hypoalbuminemia) were identified between patients with or without reported edema events[2,d]

Dose Modification Due to Edema,

Subset of Patients with Edema (n=40)[1,a]

Delayed	Reduced	Discontinued
17.5% (n=7)	2.5% (n=1)	10% (n=4)



5 of **8** patients (**63%**) who had a dose delay due to edema were rechallenged with Lonca[2,d]

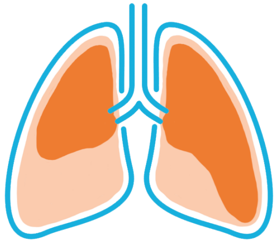
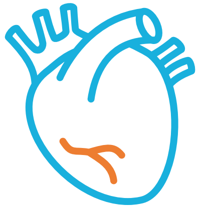
[a]Data cut-off: March 1, 2021. Post-hoc analysis.
[b]Edema includes edema, face edema, generalized edema, peripheral edema, ascites, fluid overload, peripheral swelling, swelling, and swelling face.
[c]Missing end dates were imputed using the date of new anticancer therapy (NAT) for patients who received NAT or the end of study (EOS)/data cutoff date for patients who did not receive NAT for the calculation of the duration of adverse events. Partial end dates were imputed using the last month or day of a month bounded by EOS. Grade ≥3 duration calculated at the time of first occurrence to the adverse event resolved to grade ≤2.
[d] Data cutoff: April 6, 2020. Post-hoc analysis.

REFERENCES

Dose Modification Recommendation

THERAPEUTICS

Dose Modification Recommendation in the Lonca Prescribing Information

Pleural effusion	Pericardial effusion	Edema
		
For grade 2 or higher pleural effusions (symptomatic, intervention indicated [e.g., diuretics or therapeutic thoracentesis]), withhold loncastuximab tesirine until the toxicity resolves to ≤ grade 1 (asymptomatic, clinical, or diagnostic observation only; intervention not indicated)[1,2]	For grade 2 or higher pericardial effusions (asymptomatic effusion of a small to moderate size), withhold loncastuximab tesirine until the toxicity resolves to ≤ grade 1[1,2]	For grade 2 or higher edema (edema interfering with activities of daily living; oral therapy initiated), withhold loncastuximab tesirine until the toxicity resolves to ≤ grade 1 (noted on exam; 1+ pitting edema)[1,2]

If dosing is delayed by more than 3 weeks due to toxicity related to loncastuximab tesirine, reduce subsequent doses by 50%. If toxicity reoccurs following dose reduction, consider discontinuation[1]

REFERENCES

Management of Effusion and Edema

Management of Effusion and Edema in Patients Treated with Lonca

Patient counseling in Lonca prescribing information

Advise patients to contact their healthcare provider if they experience shortness of breath or difficult, labored breathing[1]

Management in the LOTIS-2 study

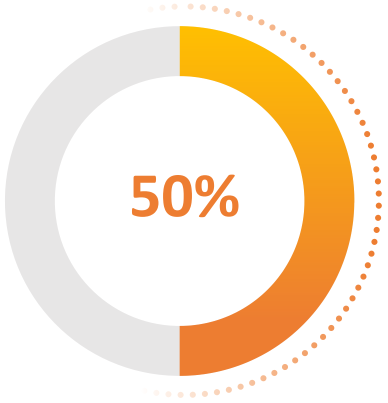
For patients with weight gain greater than 1 kg from cycle 1 day 1, new or worsening edema, and/or new or worsening pleural effusion in LOTIS-2, spironolactone at standard doses was administered (titrated as clinically indicated)[2]

- Additional diuretic support was added for further increase in weight, edema, or pleural effusion[2]

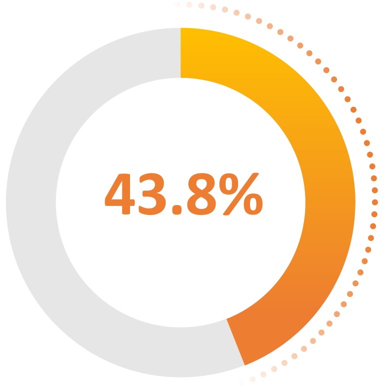
Patient counseling in the LOTIS-2 study

Patients were advised to monitor their weight on a daily basis, at around the same time (preferably in the morning), and to notify their healthcare provider if they gained >1 kg (2.2 pounds) over baseline [2]

Diuretic Therapy in the LOTIS-2 Study



Diuretic therapy (bumetanide, furosemide, or spironolactone) was administered to 20 of 40 patients (50%) with any grade edema[3,a]



Diuretic therapy was administered to 7 of 16 patients (43.8%) with any grade effusion[3,a]

[a]Data cut-off: April 6, 2020. Post-hoc analysis.

Summary

- The prescribing information for Lonca includes a warning for effusion or edema; serious effusion and edema have occurred in patients treated with Lonca[1]
- Dexamethasone premedication is recommended to reduce the incidence and severity of pyrrolobenzodiazepine (PBD)-related adverse reactions, such as effusion and edema[2,3]
- Grade ≥3 effusion or edema occurred in <5% of patients in the LOTIS-2 trial and typically occurred later in therapy than any grade effusion or edema[2]
- Among patients with edema in the LOTIS-2 trial (n=40), most presented with peripheral edema (72.5%) and facial edema (17.5%)[2]
- In the LOTIS-2 trial, diuretic therapy (bumetanide, furosemide, or spironolactone) was administered to 7 of 16 patients (43.8%) with any grade effusion and to 20 of 40 patients (50%) with any grade edema[2]
  - Dose delays, reductions, and discontinuations occurred due to effusion in 11.8%, 0%, and 23.5% of patients who experienced effusions (n=17), respectively[4]
  - Dose delays, reductions, and discontinuations occurred due to edema in 17.5%, 2.5%, and 10% of patients who experienced edema (n=40), respectively[4]

REFERENCES